REMARKS

The Applicants' below-named representative would like to thank Examiner Vera Afremova for the helpful and courteous discussion of the issues in this application held on January 26, 2005. This discussion focused on the differences between the present invention and the prior art relied upon in the outstanding Office Action. The substance of this discussion is summarized and further expanded upon in the following remarks.

The present invention is directed to an aqueous ready to use semen extender composition. The semen extender composition includes about 0.1 wt.% to about 6 wt.% phospholipid obtained from non-animal source, about 0.0001 wt.% to about 1 wt.% of surfactant to reduce ice crystal formation during freezing of the composition, about 0.5 wt.% to about 3 wt.% carbohydrate, about 3 wt.% to about 14 wt.% freeze agent comprising polyol, and biological buffer to provide the composition with a pH of about 6.9 to about 7.5, and a sufficient amount of water so that the composition exhibits an osmolality of about 250 mOsM to about 350 mOsM. The claimed invention is additionally directed to a method for manufacturing an aqueous ready to use semen extender composition.

One advantage of the aqueous ready to use semen extender composition according to the present invention is the ability to avoid the use of egg yolk which is a common component in conventional semen extender compositions while providing a semen extender composition that provides a desired level of viability and motility of the sperm cells. It is believed that egg yolk may contain nonpathogenic organisms or pathogenic organisms that may be harmful to the host or cells that contact the product. Accordingly, eliminating egg yolk from the ready to use semen extender composition reduces the risk of contamination of the semen by organisms that may be present in the egg yolk.

The specification of the above-identified patent application includes data demonstrating that the present invention preserves semen comparable to a composition that utilizes egg yolk. The Examiner's attention is directed to example 2 of the above-identified patent application. In particular, tables 8 and 9 on page 19 of the above-identified patent application demonstrate that compositions formulated as aqueous ready to use semen extender compositions containing buffer, carbohydrate, phospholipid (lecithin), and surfactant perform comparable to a semen extender composition containing egg yolk. Accordingly, the Applicants have developed a semen extender composition that can be used in place of semen extender compositions containing egg yolk.

The prior relied upon in the outstanding Office Action fails to disclose or suggest a ready to use semen extender composition or a method for manufacturing a ready to use semen extender composition according to the present invention.

Prior Art-Based Rejections

The outstanding Office Action includes three prior-art based rejections. Claims 1, 2, 6, 8, 11-14, 21, 22, 27, and 32 stand rejected under 35 U.S.C. §102(b) over EP 0 685 556 (*Ghazarian et al.*). Claims 1, 2, 4-6, 8, 10-14, 21, 22, 27, and 32 stand rejected under U.S.C. §102(e) over U.S. Patent No. 6,368,786 (*Saint-Ramon et al.*). Claims 1, 2,4-6, 8-14, 21, 22, and 24-32 stand rejected under 35 U.S.C. §103(a) over *Ghazarian et al.* or *Saint-Ramon et al.* and U.S. Patent No. 3,444,039 (*Rajamannan*), U.S. Patent No. 6,130,034 (*Aitken*), U.S. Patent No. 6,140,121 (*Ellington et al.*), and C. Helleman and E. Gieroux, Deep Freezing of Rabbit Sperm, Effect of a Surfactant on Fertilizing Capacity, Zuchthyg., 23, 33-37 (1988) (*Hellemann et al.*). These rejections are traversed.

Rejection Under 35 U.S.C. §102(b) Over *Ghazarian et al.*

The claimed invention is not anticipated by *Ghazarian et al.*

Ghazarian et al. fail to disclose a composition comprising about 0.001 wt.% to about 1 wt.% surfactant to reduce ice crystal formation during freezing of the composition. The outstanding Office Action contends that the TRIS component disclosed by *Ghazarian et al.* satisfies the surfactant component of the claimed composition. It is pointed out that *Ghazarian et al.* characterize TRIS as a buffer. See example 1 of *Ghazarian et al.* The presently claimed semen extender composition includes a "biological buffer" component and, as described by the above-identified patent application at page 7, lines 1-8, TRIS is an exemplary biological buffer that can be used in the present invention as the biological buffer component. Clearly, the above-identified patent application is not identifying TRIS as both the biological buffer component and as the surfactant component capable of reducing ice crystal formation during freezing of the composition.

Furthermore, the outstanding Office Action fails to demonstrate that TRIS would function but as a surfactant capable of reducing ice crystal formation according to the present invention. It is submitted that it is not enough that TRIS can be characterized as a surfactant. Instead, it is necessary to establish that TRIS would function as a surfactant capable of reducing ice crystal formation during the freezing of the composition as required by the presently claimed invention. The outstanding Office Action fails to satisfy this burden.

The above-identified patent application discusses the surfactant component at page 6, lines 4-31. Various surfactants are identified that can be used to reduce ice crystal growth during the freezing process and to help strength the cell membrane during the freezing and thawing process.

It is submitted that it is improper claim construction for the outstanding Office Action to contend that TRIS satisfies both the buffer component and the surfactant component of the presently claimed invention without any evidence to demonstrate that TRIS reduces ice crystal growth during the freezing process. The above-identified patent application clearly identifies TRIS as a biological buffer and not as a surfactant capable of reducing ice crystal formation during the freezing of the semen extender composition.

In view of the above comments, the claimed invention is not anticipated by *Ghazarian et al.* and withdrawal of the rejection over *Ghazarian et al.* is requested.

Rejection Under 35 U.S.C. §102(e) Over *Saint-Ramon et al.*

It is submitted that *Saint-Ramon et al.* is not available as prior art under 35 U.S.C. §102(e) against the above-identified patent application.

The above-identified patent application is entitled to a priority date of January 12, 2001 in view of U.S. Provisional Patent Application Serial No. 60/261,528. *Saint-Ramon et al.* was filed in the United States on May 11, 2000, and claims priority to a French patent application filed in France on May 14, 1999. It is unclear from the first page of *Saint-Ramon et al.* whether they are entitled to the priority date of May 14, 1999. Nevertheless, the Applicants are able to demonstrate a reduction to practice of the above-identified patent application prior to May 14, 1999. Enclosed is a Declaration under 35 U.S.C. §1.131, by Dr. Richard Lomneth, that demonstrates possession of the invention of the above-identified patent application as a result of a reduction to practice of the invention prior to May 14, 1999. The enclosed Declaration is unexecuted. The executed Declaration will be filed within several days.

In view of the enclosed Declaration under 35 U.S.C. §1.131, *Saint-Ramon et al.* does not qualify as prior art under 35 U.S.C. §102(e), and withdrawal of the rejection over *Saint-Ramon et al.* is requested.

Rejection Under 35 U.S.C. §103(a) Over *Ghazarian et al.* or *Saint-Ramon et al.* in view of *Rajamannan, Aitken, Ellington et al.*, and *Hellemann et al.*

For the reasons discussed above, U.S. Patent No. 6,368,786 to *Saint-Ramon et al.* is not available as a prior art reference under 35 U.S.C. §103(e) against the above-identified patent application. Accordingly, withdrawal of the rejection as it relates to *Saint-Ramon et al.* is requested.

Ghazarian et al. fail to disclose several of the features of the presently claimed invention. It appears that the outstanding Office Action relies upon various disclosures in several secondary references to piece together a rejection under 35 U.S.C. §103. When relying on numerous references, there must be a suggestion to combine the references or make the modifications. In re Mayne, 104 F.3d 1339, 41 USPQ2d 1451 (Fed. Cir. 1997), and In re Jones, 958 F.2d 347, 21 USPQ2d 1941 (Fed. Cir. 1992). The outstanding Office Action fails to identify a sufficient suggestion to combine the references or make the modifications. Accordingly, the outstanding Office Action fails to establish a *prima facie* case of obviousness.

Ghazarian et al. are directed to a vehicle for nonautonomous microorganisms of the animal kingdom to be kept alive outside their natural environment with a view to human interventions. The vehicle includes an aqueous medium comprising nutrition agents, buffers and mineral salts, and a protective product formed as a support for embryonic growth by a living organism, wherein the protective product is a lecithin extracted from soy seeds and introduced

into the aqueous medium upon formation of the vehicle. See the English language translation of *Ghazarian et al.* on page 2, lines 1-17, and page 3, lines 20-27.

As discussed above, *Ghazarian et al.* fail to disclose a composition containing about 0.0001 wt.% to about 1 wt.% of surfactant to reduce ice crystal formation during freezing of the composition. The outstanding Office Action contends that the TRIS component disclosed by *Ghazarian et al.* satisfies the surfactant component of the claimed composition. It is pointed out that *Ghazarian et al.* characterize TRIS as a buffer. See Example 1 of *Ghazarian et al.* The presently claimed semen extender composition includes a "biological buffer" component and, as described by the above-identified patent application at page 7, lines 1-8, TRIS is an exemplary biological buffer that can be used in the claimed composition. Clearly, the above-identified patent application is not identifying TRIS as both the biological buffer component and the surfactant component according to the presently claimed invention.

The Examiner's attention is directed to the specification of the above-identified patent application at page 6, lines 4-31, and page 7, lines 1-8. Clearly, TRIS is characterized as a biological buffer and not as a surfactant. Furthermore, the specification at page 6, lines 4-31 identify the surfactant component and characterize the surfactant component as being capable of reducing ice crystal growth during the freezing process and to help strengthen the cell membrane during the freezing and thawing process. Clearly, TRIS is not identified as an exemplary surfactant that reduces ice crystal formation during the freezing of the composition according to the present invention. Furthermore, the outstanding Office Action fails to provide any evidence showing that TRIS functions to reduce ice crystal formation during the freezing of a semen extender composition. Accordingly, the requirement of the presence of a surfactant in an amount

of about 0.0001 wt.% to about 1 wt.% to reduce ice crystal formation during the freezing of the composition according to the present invention is missing from *Ghazarian et al.*

Rajamannan appears to be relied upon in the outstanding Office Action for the disclosure of buffering to a pH of 6 to 7.5 and for the disclosure of sodium citrate as a buffering agent. See *Rajamannan* at column 3, line 30 and lines 41-47. It is pointed out that *Rajamannan* is directed at an egg yolk containing composition. See *Rajamannan* at column 1, lines 13-19, and the example disclosing the presence of egg yolk solids. It is pointed out that *Rajamannan* fails to disclose or suggest the use of a surfactant to reduce ice crystal formation during freezing of the composition according to the present invention.

It appears that the outstanding Office Action relies upon *Aitken* for the disclosure of an anti-oxidant. *Aitken* relies upon the disclosure of an anti-oxidant such as vitamin E at column 1, line 50. It is pointed out, however, that Aitken is directed at an egg yolk-containing system. See *Aitken* at column 1, lines 28-38. The outstanding Office Action fails to explain why one having ordinary skill in the art would look to a disclosure relating to the use of raw egg yolk for a suggestion to modify a composition that is free of raw egg yolk.

It is submitted that raw egg yolk contains a large number of various components and is a much more complicated system than the semen extender composition that does not contain raw egg yolk. Accordingly, the disclosure of the use of an anti-oxidant in a raw egg containing semen extender composition in no way suggests the use of an anti-oxidant in a non-raw egg containing semen extender composition.

The outstanding Office Action appears to rely on *Ellington et al.* for the disclosure of various buffers such as EDTA and TRIS. See *Ellington et al.* at column 16, lines 52-63, and column 19, line 28. The outstanding Office Action additionally refers to *Ellington et al.* for the

disclosure of a balanced culture medium such as M199 at column 16, line 59, and contends that medium M199 suggest the use of polyoxyethylene sorbitan (Tween 80). It is submitted that Tween 80 is provided in medium M199 to help dissolve other components in medium M199. There is no disclosure by *Ellington et al.* or ATCC Catalogue (Page 522) disclosing or suggesting that Tween 80 can be used to reduce ice crystal formation during freezing of a semen extender composition.

It is submitted that the reliance upon *Ellington et al.* and ATCC Catalogue (Page 522) is an example of the use of impermissible hindsight. There must be a suggestion to combine the references or make the modifications to achieve a *prima facie* case of obviousness. It is not enough to simply pick and choose various components from several references.

Hellemann et al. are apparently relied upon in the outstanding Office Action for the disclosure of sodium laurel sulfate in a composition intended for rabbit semen. See the abstract of *Hellemann et al.* Similar to *Aitken*, *Hellemann et al.* are directed at the use of a composition containing raw egg. It is submitted that one having ordinary skill in the art would not have looked to *Hellemann et al.* for modifying a composition that does not contain raw egg yolk.

In view of the comments, the presently claimed invention would not have been obvious from *Ghazarian et al.*, *Saint-Ramon et al.*, *Rajamannan*, *Aitken*, *Ellington et al.*, and *Hellemann et al.* Accordingly, withdrawal of this rejection is requested.

Rejection Under 35 U.S.C. §112

Claims 24, 25, 28, and 29 stand rejected under 35 U.S.C. §112, second paragraph in view of the term "IU." This rejection is traversed.

The unit of measurement "IU/ml" is a commonly used measure of concentration. The Examiner's attention is directed to the following exemplary publications that disclose the use of the unit "IU/ml":

U.S. Patent No. 6,595,762

Exp Gerontol. 1991; 26 (4): 365-74.

Enclosed are excerpts from both publications disclosing the use of the unit "IU/ml." Clearly, one having ordinary skill in the art would understand that the unit "IU/ml" is commonly used and withdrawal of this rejection is requested.

Claims 25 and 29 stand rejected under 35 U.S.C. §112, first paragraph. In view of the above amendment to claims 25 and 29, it is believed that this rejection has been rendered moot. Accordingly, withdrawal of this rejection is requested.

It is believed that this application is in condition for allowance. Early notice to this effect is earnestly solicited.

Respectfully submitted,

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http://www.pharmcast.com/Patents/Yr2003/July2003/072203/6596762_Antioxidant072203.htm

patent 6,595,762

In one aspect, the invention consists of a formulation of antioxidants that include: a water soluble form of vitamin E (e.g., D-alpha tocopheryl polyethelene glycol-1000 succinate, or TPGS) at a concentration from about **20 IU/ml to about 75 IU/ml**; mixed carotenoids at a concentration from about 0.1 mg/ml to about 0.75 mg/ml; and selenium at a concentration of from about 1 .mu.g/ml to about 5 micrograms/ml (.mu.g/ml). Concentrations are described herein as an amount of the given compound per milliliter of the composition as a whole. This mixture of antioxidants are all targeted to the liver and will be well absorbed from the intestines even in the presence of significant liver dysfunction. This particular mixture of antioxidants provided in the indicated amounts is believed to be effective in preventing the fibrosis and cirrhosis of non-alcoholic steatohepatitis (NASH), thereby reducing the symptoms of the condition.

Exp Gerontol. 1991;26(4):365-74. Related Articles, Links

Effect of vitamin E on the accumulation of fluorescent material in cultured cerebral cortical cells of mice.

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The effect of vitamin E on the accumulation of lipofuscin-containing fluorescent material in the mouse cerebral cortical cells in primary culture was studied. Fluorescent material was extracted in ethanol:diethylether (3:1) and autofluorescence intensity of the extracts was measured by a spectrofluorophotometer. Although vitamin E at the concentration of 0.005 IU/ml was not effective, 0.01 IU/ml vitamin E inhibited the accumulation of fluorescent material. Fluorescent material accumulation was reduced to 76.3-86.4% of the control level in 6-, 12-, or 18-day treatment of 0.01 IU/ml vitamin E. High doses of vitamin E (0.05 or 0.1 IU/ml) were toxic for cultured cells. Ethanol, the vehicle of vitamin E, at the fina l concentration of 0.005% was also effective on the reduction of fluorescent material accumulation (81.0% of the control level at 18 days). The inhibitory effects of vitamin E as well as ethanol on the accumulation of fluorescent material in cultured cells are explained by their nature as free radical scavengers

Int J Vitam Nutr Res. 1981;51(4):331-41. Related Articles, Links